Transfer of scientific concepts to clinical practice: recent robot-assisted training studies

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Summary

The annual incidence of stroke in industrialised countries is approximately 180 per 100,000 inhabitants (1). Three months after a stroke, a third of surviving patients are still wheelchair-dependent, while gait velocity and endurance are significantly reduced in approximately 80% of those who are ambulatory (2). Restoration of motor function is a priority of post-stroke rehabilitation, the aim being to facilitate the patient’s reintegration into society (3). To achieve this goal, task-specific repetitive robot-assisted training of the upper and the lower extremity is currently the most promising approach. The main aim of conventional physiotherapy after a stroke is instead to reduce the elevated muscle tone and to practise gait preparatory tasks while sitting or standing. As a result of this, the number of steps actually taken in a single session of conventional physiotherapy may rarely exceed fifty to eighty (4).

To increase the number of steps per training session, gait machines, either applying an exoskeleton (5) or an end-effector principle (6, 7), have been developed. Traditionally, the activity of commercially available gait machines has been limited to the repetitive exercise of walking on the floor. Now, however, newer end effector-based walking robots (8) are appearing which have fully programmable trajectories and also enable harness-secured and partially body weight-supported patients to gain repetitive stair-climbing practice (both climbing and descending stairs).

This review of the literature to date looks at the most important results of clinical studies using the most common robotic systems for rehabilitation of the upper and the lower extremities.

Upper extremity robotic systems

Robotic systems for the upper extremity can be divided into end effector-based systems and exoskeletons.

End effector-based systems

The MIT-Manus (14) is considered the pioneer of robotic devices for the upper extremity. A clinical trial to test the safety and efficacy of this device (13) is currently in progress and its results are expected in early 2010. In this study, 128 participants (96% males, mean age 65 years) presenting upper extremity impairment more than six months after a stroke (ischaemic in 85% of cases) were randomly assigned to robot-assisted therapy (49 patients), intensive comparison therapy (50 patients), or usual care (28 patients). Robot-assisted therapy and intensive comparison therapy each consisted of three
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The primary outcome in this study was the Fugl-Meyer (Fugl-Meyer 0-68) assessment at 12 weeks relative to baseline (the mean Fugl-Meyer score at entry was 18.9), while Wolf Motor Function Test and Stroke Impact Scale scores were among the secondary outcomes. Fifty-eight per cent of strokes occurred in the anterior circulation and 20% of the participants reported a stroke in addition to their index stroke. The average time from the index stroke to enrolment was 56 months (range: 6 months to 24 years).

A very recent study (14) was conducted with the aim of testing the performance of linear regression models in estimating clinical scores for the upper extremity from systematic robot-based metrics. Twenty kinematic and kinetic metrics were derived from movement data recorded, using the MIT-Manus device, from 111 chronic stroke patients. Multiple linear regression models were developed to calculate Fugl-Meyer, motor status, motor power, and Modified Ashworth Scale scores from these robot-based metrics. The best performance-complexity trade-off was achieved by the motor status score model based on eight kinematic macro-metrics. Models that included kinematic micro-metrics did not achieve significantly higher performances. The performances of the Modified Ashworth Scale models were consistently low.

Another shoulder-elbow robotic device is the Mirror Image Movement Enabler (MIME) (15), which applies forces to the paretic limb during unilateral and bilateral movements in three dimensions. A randomised controlled clinical trial of the MIME in shoulder and elbow neurorehabilitation was carried out in subacute stroke patients; data on its use in bilateral training mode were also gathered. Robot-assisted treatment (bilateral, unilateral, and combined bilateral and unilateral) was compared with conventional therapy. In line with the findings of a previous study in chronic stroke, combined unilateral and bilateral robotic training showed advantages compared with conventional therapy, producing larger improvements on a motor impairment scale and a measure of abnormal synergies. However, gains in all treatment groups were equivalent at the six-month follow up. Combined unilateral and bilateral training yielded functional gains that were similar to the gains from equivalent doses of unilateral-only robotic training, although the combined group had more hypertonia and less movement out of synergy at baseline.

A simpler end effector-based robot is the NeReBot (16), which passively moves the paretic arm in three dimensions. A clinical trial of this device was conducted in 20 patients with post-stroke hemiparesis or hemiplegia submitted to standard post-stroke multidisciplinary rehabilitation and randomly assigned to exposure to the robotic device either without or with four weeks’ preliminary sensorimotor robotic training (about 4 hours/week). This training consisted of peripheral manipulation of the shoulder and elbow of the impaired limb, correlated with visual stimuli. On discharge from hospital, impairment and disability had declined in all the patients, but the robot training group recorded higher gains in the areas of motor impairment and functional recovery, which were maintained at three months. No adverse events resulted from robot-assisted therapy in either group.

The BiManuTrack (17) is another end effector-based robot for the upper extremity; the difference is that this device works on more distal arm movements, practising bilateral prosupination and flexion/extension of the wrist. In a clinical trial, 44 patients with severe arm paresis (Fugl-Meyer Motor Score lower than 18) four to eight weeks after stroke were randomly assigned to six weeks of robot-assisted therapy or six weeks of electrical stimulation: one 20-minute session per weekday, each session consisting of 800 repetitions with the robot or 60-80 wrist extensions, respectively. The primary outcome measure was the blindly assessed Fugl-Meyer, and the secondary measures were upper limb muscle power [Medical Research Council (MRC) sum, 0 to 45] and muscle tone (Ashworth score sum, 0 to 25), assessed at the beginning and end of treatment and at the three-month follow up. With the exception of a higher Barthel Index score at baseline recorded in the robot-assisted therapy group (found to have no influence), the groups were homogenous. The Fugl-Meyer and MRC sum scores improved over time in both groups but the improvement was significantly greater in the robot-assisted therapy group. The Fugl-Meyer score at the end of the study and at the three-month follow up was 15 points and 13 points higher in the robot-assisted therapy group than in the control group, while the MRC sum score was 15 points higher at both time points compared with the electrical stimulation control group. Muscle tone remained unchanged, and no side effects were reported.

The possibility of combining robotics with transcranial direct stimulation (tDCS) is an interesting new option in this field. The findings of the pilot study in which this technique was combined with BiManuTrack (18) suggest that central stimulation may enhance the effect of conventional physical therapies after stroke. The use of tDCS with robot-assisted arm training was examined in a pilot study in 10 patients who had suffered an ischaemic stroke 4-8 weeks before the study onset and who had no history of epilepsy. Eight had a cortical lesion and two had subcortical lesions; all had severe arm paresis and, coincidentally, five had severe aphasia. Over six weeks, they received thirty 20-minute sessions of robot-assisted arm training. During the first seven minutes, tDCS (1.5mA) was applied, with the anode placed over the lesioned hemisphere and the cathode above the contralateral orbit. Arm and language impairment were assessed using the Fugl-Meyer and the Aachener Aphasia Test, respectively. No major side effects occurred. The arm function of three patients (two with a subcortical lesion) improved significantly, their Fugl-Meyer scores increasing from 6 to 28, 10 to 49 and 11 to 48. The remaining seven patients, all with cortical lesions, showed little change in their arm function, their Fugl-Meyer scores failing to increase by more than five points. Unexpectedly, aphasia improved in four patients.

**Exoskeleton systems**

Exoskeleton systems are an alternative to end effector-based systems, and the first results of clinical studies conducted using exoskeletons are now becoming available. Compared to end effector-based robots, exoskeletons provide improved guidance of the human limb and are able to train task-oriented movements with a large range of motions.

In a recent study, the feasibility of using the ARMin ro-
robotic rehabilitation device (arm exoskeleton) in chronic stroke patients was tested (19). Three single cases with chronic hemiparesis at least 14 months after unilateral stroke underwent two weeks of multiple baseline measurements, eight weeks of training with repetitive measurements and a follow-up measurement eight weeks after the end of the training. The training programme included shoulder and elbow movements with the ARMin. Two subjects had three one-hour sessions per week and one subject received five one-hour sessions per week. The upper-limb part of the Fugl-Meyer assessment was taken as the main outcome measurement. The ARMin training was well tolerated by all the patients, three of whom recorded moderate but significant Fugl-Meyer score improvements. Most improvements were maintained eight weeks after discharge.

The ARMOR electromechanical arm robot (20) is a more complex exoskeleton system with a bilateral approach. Developed to promote motor rehabilitation of the upper limb, it is capable of moving all joints through complex patterns. Eight patients following stroke of different aetiologies were included in a clinical AB-BA crossover study comparing ARMOR training with EMG-triggered neuromuscular electrical stimulation (EMG-NMES). Chedoke-McMaster Stroke Assessment, modified Ashworth Scale, goniometry, dynamometry and the Functional Dexterity Test were used as outcome measures. Compared with the EMG-NMES, the ARMOR training was associated with more improvement of muscle tone, range of movement and dexterity, but less improvement of strength. The Chedoke-McMaster Stroke Assessment showed improvements of at least one point in shoulder pain and arm and hand activity with the ARMOR training, whereas these values did not change with the EMG-NMES.

Another bilateral exoskeleton system, similar to the ARMOR, is Aramis (21). This system, which is still in the prototype stage and needs to be validated in clinical studies, allows the therapist to design neurorehabilitation training protocols in which sample exercises are generated by a single exoskeleton operated by the patient’s unaffected arm or by the therapist’s arm and mirrored in real-time or offline by the exoskeleton supporting the paretic arm.

Lower extremity robotic systems

Robotic systems for the lower extremity can also be divided into end effector-based systems and exoskeletons.

End effector-based systems

One simple end effector for gait rehabilitation is the electromechanical gait device, LokoHelp (7). In a neurological rehabilitation centre for children, adolescents and young adults, six patients with impaired gait (two after stroke, two after spinal cord injury and two after brain injury) were enrolled in a first study. Over the six-week study period they underwent twenty training sessions on a treadmill fitted with LokoHelp and providing body weight support. Their progress was assessed with the following instruments: the Functional Ambulation Category (FAC) (walking ability), the 10-metre walk test (gait velocity), the Motricity Index (lower limb strength), the Berg Balance Scale (postural capacity), the modified Ashworth Scale (spasticity) and the Rivermead Mobility Index (activity). No severe adverse events were observed during the locomotion training with LokoHelp. The patients showed improved walking ability, lower limb strength, postural capacity and activity. The training intensity had to be adjusted in one patient who complained of knee pain.

The most popular end effector device is the Gang- Trainer GT1 (22). In a multicentre trial involving four German neurological rehabilitation centres 155 non-ambulatory patients (first-time stroke <60 days) were divided into two groups. Every weekday for four weeks group A received 20 minutes of locomotor training with this device plus 25 minutes of physiotherapy, while group B received 45 minutes of physiotherapy. Primary variables were the FAC and the Barthel Index, blindly assessed at study onset, study end, and at six-month follow up. Responders to the therapy had to become ambulatory or reach a Barthel Index higher than or equal to 75. Secondary variables were walking velocity, endurance, mobility and leg power. The intention-to-treat analysis revealed that a significantly greater number of the patients receiving locomotor training (group A) were able to walk independently at treatment end: 41 out of 77 versus 17 out of 78 in group B. Also, significantly more group A patients had reached a Barthel Index higher than or equal to 75: 44 out of 77 versus 21 out of 78. At six months, the superior gait ability recorded in group A persisted. As regards the Barthel Index the number of responders increased to 45 in group A and to 36 in group B. The group A patients recorded significantly greater improvements in all secondary variables during the treatment period, but not during the follow up.

The positive results of training with end effector-based machines were confirmed by a Cochrane report (23) on the effect of automated electromechanical and robotic-assisted gait training devices for improving walking after a stroke. The review included eight trials with a total of 414 participants. Electromechanical assisted gait training in combination with physiotherapy was found to increase the odds of achieving independent walking and increased walking capacity, but did not significantly increase walking velocity. However, the authors pointed out that these results must be interpreted with caution in view of the variations that emerged between the trials (differences in treatment duration and frequency and in the ambulatory status of patients; moreover, some trials tested electromechanical devices in combination with functional electrical stimulation).

Devices with programmable footplates are now opening up new frontiers in gait rehabilitation. An early device of this kind was the HapticWalker (24) for gait training along arbitrary daily life walking trajectories. However, because of its dimensions and high electrical power consumption, this machine had no clinical applicability and was replaced by the G-EO-Systems. The G-EO-Systems was recently used in a study evaluating the muscle activation pattern of eight lower limb muscles, measured using dynamic electromyography, in six hemiparetic patients during free and simulated walking on the floor and during stair climbing. For the floor walking task, the pattern of the thigh muscles was comparable during the real and simulated conditions across
all subjects. Minimal deviations were a delayed onset and a prolongation of the activation of the vastus medialis and lateralis during the simulated walking (data not yet published).

Due to the higher gait velocity of the Haptic Walker, the quality of the training it provides can be investigated in healthy subjects during free floor walking and stair climbing; or during the same tasks in two different HapticWalker training modes: with and without vertical centre of mass movement. In a study by Hussein et al. electromyograms of eight gait relevant muscles were measured and muscle activation was compared for the different training modes. The study, which used muscle activation as an indicator of the quality of rehabilitation training, investigated whether cancellation of the vertical centre of mass movement by adaptation of the foot-plate trajectory is feasible and whether the muscle activation patterns on the HapticWalker agree. The results showed no significant differences in activation timing (24).

**Exoskeleton systems**

The most well-known exoskeleton is the Lokomat (5). In the most recent study to use this system (25) 16 volunteers with chronic hemiparetic gait post-stroke were randomly allocated to Lokomat or manual body weight-supported treadmill training three times a week for four weeks. The groups were also stratified by fast or slow training speeds. The primary outcomes were self-selected overground walking speed and paretic step length ratio. Secondary outcomes included: fast overground walking speed, six-minute walking test, and a battery of clinical measures. No significant differences in primary outcomes emerged between the Lokomat and manual training manual groups at the end of the four weeks. However, within the Lokomat group, improvements were recorded in self-selected walking speed, paretic step length ratio, and four of the six secondary measures. Within the manual group, only balance scores improved. No differences were found between the fast and slow training groups.

Another multicentre randomised trial (26) compared, for efficacy, Lokomat-assisted gait training and conventional gait training in individuals with subacute stroke. A total of 63 participants less than six months post-stroke with an initial walking speed of between 0.1 and 0.6 m/s completed the trial. All participants received 24 one-hour sessions of either Lokomat or conventional gait training. Outcome measures were evaluated prior to training, after 12 and 24 sessions, and at a three-month follow-up examination. Self-selected overground walking speed and distance walked in six minutes were the primary outcome measures, whereas the secondary outcome measures included balance, mobility and function, cadence and symmetry, level of disability, and quality of life measures. Participants who received conventional gait training experienced significantly greater gains in walking speed and distance than those trained on the Lokomat. These differences were maintained at the three-month follow-up evaluation. Secondary measures did not differ between the two groups, although a two-fold greater improvement in cadence was observed in the conventional versus the Lokomat group.

**Discussion**

The higher treatment intensity achieved using robot-assisted therapy is the most likely explanation for the enhanced results recorded in the upper extremities. Indeed, the achievement of a high number of repetitions has also been shown to be an effective approach in other therapeutic settings, with several clinical studies reporting that sessions of repetitive therapy can lead to improvement of motor functions in stroke and other neurological disabilities (27). However, the contribution, to outcome, of robotic therapy per se is still unclear.

In particular, the bilateral approach, compared with unilateral paretic hand movement, has been shown to enhance activation in stroke patients in the early recovery stage. The possibility of improvements in proximal and distal motor control suggests that the effect of the treatment is generalised. It can be speculated that the more distal approach resulted in more powerful activation of the sensorimotor cortex given the larger cortical representation of the hand. The recently suggested competition between proximal and distal arm segments for plastic brain territory after stroke would recommend shifting the emphasis of treatment from the shoulder to the forearm, hand, and fingers.

Exoskeleton systems are still too recent to have been the subject of robust clinical trials, although studies evaluating the effects of therapy using these systems are in progress.

As regards the lower extremities, it has been shown that stroke patients receiving electromechanical assisted gait training in combination with physiotherapy are more likely to achieve independent walking than patients receiving gait training without the use of these gait training devices. However, further research should address specific questions, for example, what might be the most effective frequency or duration of electromechanical assisted gait training, and how soon after stroke should it begin? Follow-up studies are also needed to find out how long the benefits last.

The new option of free programmable footplates, able to reproduce every possible situation in gait adds new therapeutic opportunities to the already widely demonstrated benefits of end effector devices and this aspect needs to be further explored in vigorous clinical studies. One limitation of exoskeleton systems is the fact that they need a treadmill for the stance phase, which makes it impossible to obtain a machine suitable for trajectories other than walking on the floor. Although clinical results obtained with exoskeleton systems differ, as with end effector-based systems the value of using these therapies in addition to conventional physiotherapy seems to be emerging.

**References**

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